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9/1/09 Michelle Hobson
Date Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:	Examiner: J. Dunston
CHOO et al.	Group Art Unit: 1636
Serial No.: 09/996,484	Confirmation No.: 2713
Filing Date: November 28, 2001	Customer No.: 20855
Title: MOLECULAR SWITCHES	

REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In accordance with 37 C.F.R. § 41.41, Appellants submit one copy of this Reply Brief in response to the Examiner's Answer. Examiner's Answers were mailed on July 8, 2009 and August 24, 2009. Accordingly, this Revised Brief is timely filed.

REAL PARTY IN INTEREST

Gendaq Ltd. is the assignee of the instant application, as recorded on August 22, 2005 in the USPTO at Reel 016655, Frame 0867. See, also, Certificate Under 37 C.F.R. § 3.73(b) filed on April 1, 2002. Gendaq, Ltd. is a wholly owned subsidiary of Sangamo BioSciences, Inc. Therefore, the real party in interest is Sangamo BioSciences, Inc.

RELATED APPEALS AND INTERFERENCES

Appellants are not aware of any related appeals or interferences.

STATUS OF CLAIMS

Pending: Claims 1, 2, 4, 5, 7, 8, 10, 11, 13-15, 21-26, 31, 34, 35 and 38-48

Canceled: Claims 3, 6, 9, 12, 16-20, 27-30, 32, 33, 36, 37, 49

Withdrawn: Claims 1, 2, 4, 5, 7, 8, 10, 11, 13-15, 21-26, 31, 35 and 38-47

Rejected: Claims 34 and 48

Appealed: Claims 34 and 48

STATUS OF AMENDMENTS

No amendments have been made subsequent to the mailing of the Final Office Action on June 4, 2008.

Appellants note that their Response after Final was mailed within 2 months of the mailing of the Final Office Action and, therefore, expedited procedure was in order. However, no Advisory Action was ever received, despite repeated telephone calls and a written status inquiry to the Office.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Whether claims 34 and 48 are unpatentable under 35 U.S.C. § 103(a) as obvious in view of WO 96/06110 (hereinafter "Gilman").

Appellants note that the Examiner's Answers withdrew the previous rejections under 35 U.S.C. § 112, 1st paragraph (written description) and 35 U.S.C. § 112, 2nd paragraph as allegedly indefinite.

ARGUMENTS

A. Claims 34 and 48 are non-obvious over Gilman

Claims 34 and 48 were rejected as allegedly obvious over WO 96/06110 (hereinafter "Gilman"). (Examiner's Answer, pages 3-6). Gilman was again cited for allegedly teaching all the claimed elements except for a non-naturally occurring Cys2-His2 zinc finger binding domain, although "non-naturally occurring" was alleged to be "impossible" to determine (Examiner's Answer page 5):

> Although Gilman et al. does not explicitly teach that the engineered Cys2-His2 zinc finger binding domain should not occur in nature and, as described above, it would be impossible to know whether any given engineered binding domain occurs in nature, Gilman et al. does teach that the engineered DNA binding domains might be selected from phage display libraries (see especially page 10, lines 13-15), which would comprise large numbers of random mutants.

However, as acknowledged by withdrawal of the rejections under 35 U.S.C. § 112, 1st and 2nd paragraphs, the term "non-naturally occurring" is not impossible to determine, but clear to the skilled artisan.

Furthermore, in response to Appellants arguments, it was asserted that Gilman's teachings are not limited to naturally occurring Cys2-His2 zinc finger domains. *See, e.g.,* page 7 of Examiner's Answer, citing page 10, lines 4-15. In addition, in response to Appellants noting that Gilman doesn't teach complexes in which heterodimerization is mediated by a ligand that binds to the DNA binding domains, it was asserted that the instant claims do not require the ligand to the bind to the first and second polypeptide. (Examiner's Answer, page 8). Likewise, with respect to the argument that Gilman only teaches covalent

linkage of DNA-binding domains, it was asserted that the paragraph bridging pages 2-3 of Gilman teaches "multimerized" DNA binding domains brought together by a ligand. (Examiner's Answer, pages 8-9, also citing page 5, lines 4-12; page 7, lines 29-31, pages 8, lines 9-19 and sentence bridging pages 7-8 of Gilman).

Contrary to the Examiner's assertions, it remains the case that the claims clearly specify that the ligand binds directly to the DNA-binding polypeptides (first and second polypeptides) to mediate heterodimerization. *See,* step (b) of claim 34, stating "a ligand that binds to the first and second polypeptides and mediates heterodimerization of the first and second polypeptides..." and lines 3-5 of claim 48 which read "wherein binding of the first polypeptide to the second polypeptide forms a heterodimer and the binding of the first and second polypeptides is mediated by binding of a ligand to the first and second polypeptides." In other words, the claims are clear that the ligand binds directly to the DNA binding polypeptides themselves rather than to a ligand-binding domain separate from the DNA-binding domains.

Indeed, the as-filed specification is silent as to ligand-binding domains. This is because the invention is directed to complexes in which the ligand is bound directly to both of the non-naturally occurring Cys2-His2 DNA binding proteins themselves (not chimeras as described in Gilman that include ligand-binding domains). *See, e.g.,* Examples regarding zinc finger DNA binding domains with no mention of additional, ligand-binding domains and page 2, lines 8-10; page 28, line 31 to page 29, line 3 of as-filed specification:

> Ligand mediated association and dissociation of proteins is also known, in which the ability of a protein to interact with another protein is dependent on the binding of a ligand to one or both proteins.
>
> Moreover, ligands which bind to a zinc finger polypeptide so as to influence zinc finger interaction and thus binding may be identified. Mutation of residues which affect the interaction between zinc fingers allows for selection of fingers which are modulatable by ligand binding at these sites.

By contrast, Gilman explicitly teaches away from the claimed complexes in which the ligand binds directly to the DNA binding polypeptides (*e.g.,* zinc finger proteins). Rather, Gilman requires that, in order to form their hypothetical multimers joined by ligand, the DNA-binding domain must be a part of a chimeric protein that further includes a ligand-binding domain. *See, e.g.,* page 2, lines 4-8; page 8, lines 11-13; page 9, line 33 to page 10, line 2 of Gilman, emphasis added:

> The multimerizer-linked composite DBPs comprise two or more chimeric proteins, each comprising at least one binding site for a multimerizing ligand, at least one component DBD, such as mentioned above and described in further detail herein, and one or more optional domains, as discussed below.
>
> The multimerizing ligand may bind to the chimeras **containing such ligand-binding domains**, in either order or simultaneously,...
>
> Of course, for embodiments involving composite DNA-binding proteins formed only upon multimerizer-mediated assembly of the protein complex, each chimeric protein contains only a subset or portion of one of the foregoing composite DBDs, together with other domains such as linker, **ligand-binding**, and other optional domains.

Thus, in Gilman's notional multimers, the ligand binds to the ligand-binding domain portion of a chimeric protein that includes separate ligand-binding and DNA binding domains. This is completely unlike the claimed invention in which a ligand mediates heterodimerization via binding directly to the zinc finger DNA binding polypeptide.

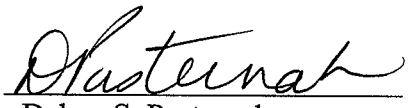
The fact remains that in order to establish obviousness of a claimed invention, all the features of the claims must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). For the reasons of record and reiterated herein, Gilman fails to teach complexes in which a ligand mediates heterodimerization of two non-naturally occurring zinc finger protein polypeptides by binding directly to these polypeptides, as claimed. Thus, since the reference does not teach the claimed elements, obviousness has not been and cannot be established and withdrawal of this rejection is in order.

CONCLUSION

For the reasons stated above, Appellants respectfully submit that the pending claims are novel and non-obvious. Accordingly, Appellants request that the rejections of the claims on appeal be reversed, and that the application be remanded to the Examiner so that the appealed claims can proceed to allowance.

Respectfully submitted,

Date: September 1, 2009

By: 

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CLAIMS APPENDIX

The claims on appeal are as follows:

34. A complex comprising:

(a) a heterodimer comprising

(i) a first polypeptide, and

(ii) a second polypeptide; and

(b) a ligand that binds to the first and second polypeptides and mediates heterodimerization of the first and second polypeptides,

wherein the first and second polypeptides bind to DNA, and further wherein the first or second polypeptide comprises an engineered, non-naturally occurring Cys2-His2 zinc finger binding domain.

48. A switching system comprising a protein switch comprising: (i) a first component comprising a first polypeptide and (ii) a second component comprising a second polypeptide, in which the first polypeptide binds to the second polypeptide, wherein binding of the first polypeptide to the second polypeptide forms a heterodimer and the binding of the first and second polypeptides is mediated by binding of a ligand to the first and second polypeptides, and (iii) a third component comprising the ligand, wherein the first and second polypeptides bind to DNA, and further wherein the first or second polypeptide comprises an engineered, non-naturally occurring Cys2-His2 zinc finger binding domain.

EVIDENCE APPENDIX

As the Examiner's Answer withdrew the rejections under 35 U.S.C. § 112, no documents are submitted with the Evidence Appendix of this Reply Brief.

RELATED PROCEEDINGS APPENDIX

As noted above on page 2 of this Appeal Brief, Applicants are not aware of any related, currently pending appeals or interferences. Accordingly, no documents are submitted with this Appendix.